Contraceptive eligibility for women at high risk of HIV: WHO guidance statement

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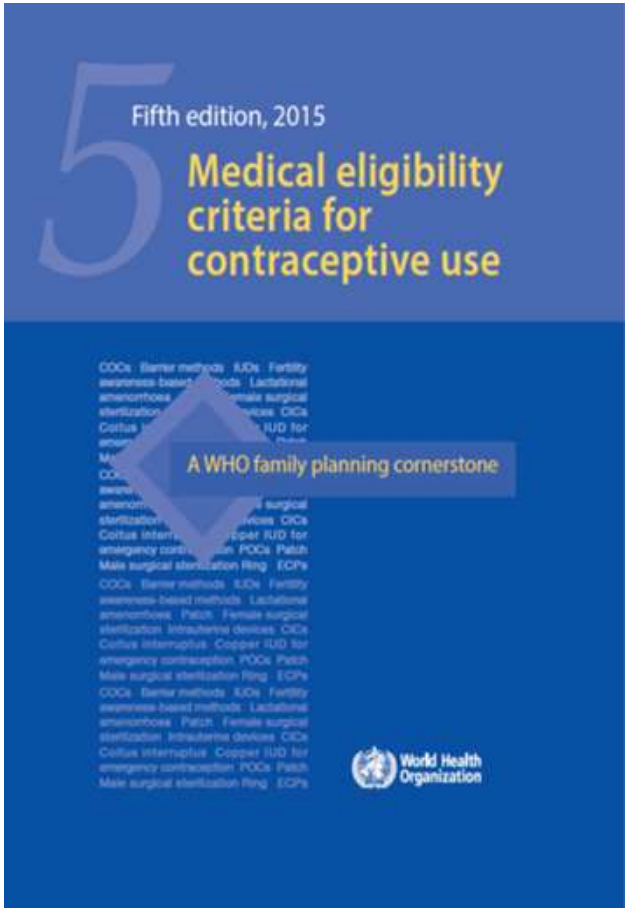
Medical eligibility criteria for contraceptive use (MEC)



- Provides recommendations (> 2000) on eligibility for 25 methods of contraception
- Conditions include:
  - A physiological status (e.g. parity, breastfeeding)
  - A group with special needs (adolescents, perimenopausal women)
  - A health problem (e.g. headache, irregular bleeding)
  - A known pre-existing medical condition (e.g. hypertension, STI, diabetes)
  - ***High risk of HIV infection***

MEC Categories

1	A condition for which there is no restriction for the use of the contraceptive method
2	A condition where the advantages of using the method generally outweigh the theoretical or proven risks
3	A condition where the theoretical or proven risks usually outweigh the advantages of using the method
4	A condition which represents an unacceptable health risk if the contraceptive method is used

Where warranted, recommendations will differ if a woman is starting a method (I = initiation) or continuing a method (C = continuation)

CATEGORY	WITH CLINICAL JUDGEMENT	WITH LIMITED CLINICAL JUDGEMENT
1	Use method in any circumstance	**YES** (Use the method)
2	Generally use the method	
3	Use of method not usually recommended unless other more appropriate method are not available or not acceptable	**NO** (Do not use the method)
4	Method not to be used	

Clarifications

- In cases where the number itself does not adequately communicate the essence of the recommendation, a clarification accompanies the numerical recommendation
  - Appears in the right hand column of the MEC document
  - Responsibility of expert working group

Hormonal contraceptive eligibility for women at high risk of HIV

2017 GUIDANCE STATEMENT

World Health Organization hrp

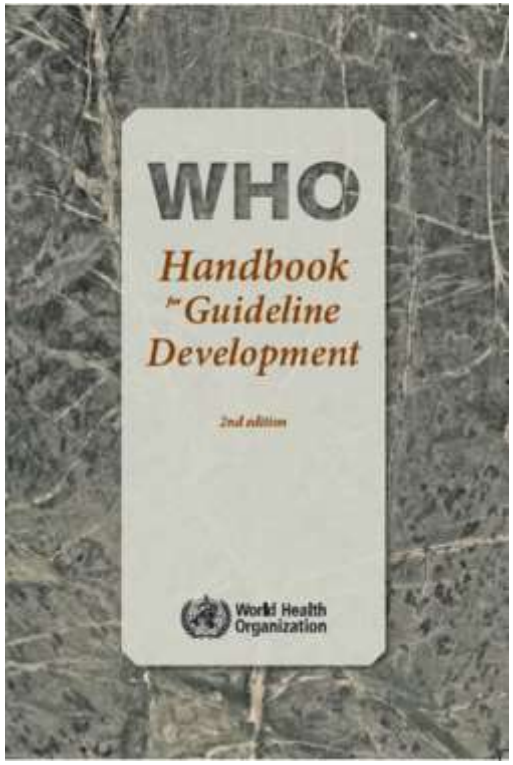
Recommendations for progestogen-only contraceptives

Condition	POP	DMPA NET-EN	LNG/ETG implants	Clarifications/evidence
POP = progestogen-only pill	LNG/ETG = levonorgestrel and etonogestrel (implants) NET-EN = norethisterone enanthate (injectable)			DMPA = depot medroxyprogesterone acetate (injectable)
High risk of HIV	1	**2**	1	**CLARIFICATION: There continues to be evidence of a possible increased risk of acquiring HIV among progestogen-only injectable users. Uncertainty exists about whether this is due to methodological issues with the evidence or a real biological effect. In many settings, unintended pregnancies and/or pregnancy-related morbidity and mortality are common, and progestogen-only injectables are among the few types of methods widely available. Women should not be denied the use of progestogen-only injectables because of concerns about the possible increased risk. Women considering progestogen-only injectables should be advised about this possible increased risk, about the uncertainty about whether there is a causal association, and how to minimise their risk of acquiring HIV.** EVIDENCE: Evidence from 13 observational studies of DMPA, NET-EN, or non-specified progestogen-only injectables, which were considered to be "informative but with important limitations",[6] continues to show some association between use of progestogen-only injectables and risk of HIV acquisition, but it remains unclear whether this results from a causal association or methodologic limitations. Two small studies assessing levonorgestrel implants, which were considered to be "informative but with important limitations", did not suggest an elevated risk, although the risk estimates were imprecise. One study reported no association between use of progestogen-only pills and HIV acquisition.

Recommendations for other methods

Condition	COC/P/R	CIC	Cu-IUD	LNG-IUD
COC = combined hormonal contraceptive P = combined contraceptive patch R = combined contraceptive vaginal ring CIC = combined injectable contraceptive Cu-IUD = copper-bearing intrauterine device (IUD) LNG-IUD = levonorgestrel-releasing IUD				
At high risk of HIV	1	1	2	2

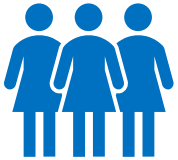
Note: The condition 'at high risk of HIV' has been classified as MEC category 2 because STI conditions are generally classified as MEC category 2 for Cu-IUD or LNG-IUD use.



WHO STANDARDS FOR GUIDELINE DEVELOPMENT

Process

Presentations providing context



Values & preferences of contraceptive users

Summary of systematic reviews

Review of the biological data

Process

Presentations providing context

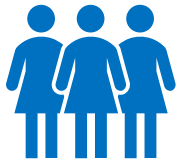
- Current WHO recommendations
- Review of implementation experience

Summary of systematic reviews

- ECHO Study results
- 2 systematic reviews:
  - Hormonal methods
  - Copper-bearing IUDs
- Review of GRADE evidence tables

Process

Values & preferences of contraceptive users



- Systematic review of published studies
- Consultative engagements with affected populations
- Perspectives from affected populations

Review of the biological data

Guideline Development Group

- Reviewed GRADE profiles;
- Used Evidence to Decision framework to formulate recommendations;
- Identified evidence gaps;
- Reviewed & approved guideline for submission to WHO Guidelines Review Committee (GRC).

Combined hormonal contraceptives: *No change*

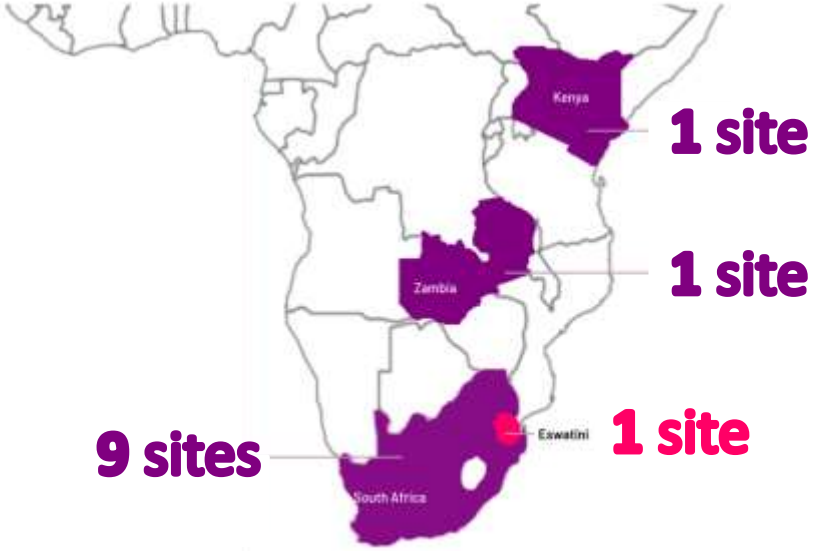
Condition	COC	P	CVR	CIC	Clarification/evidence
COC = combined oral contraceptive CVR = combined vaginal ring					P = combined contraceptive patch CIC = combined injectable contraceptive
At high risk of HIV	1	1	1	1	**Evidence**: Low-moderate quality evidence from eleven observational studies suggested no association between COC use (it was assumed that studies which did not specify OC type, examined mostly, if not exclusively, COC use) and HIV acquisition (4, 6). No studies of P, CVR or CIC were identified.

4. Polis CB, Curtis KM, Hannaford PC, Phillips SJ, Chipato T, Kiarie JN, et al. An updated systematic review of epidemiological evidence on hormonal contraceptive methods and HIV acquisition in women. AIDS. 2016;30(17):2665-83.
6. Sabo MC, Richardson BA, Lavreys L, Martin HL, Jr., Jaoko W, Mandaliya K, et al. Does bacterial vaginosis modify the effect of hormonal contraception on HIV seroconversion. AIDS. 2019;33(7):1225-30.

Progestogen-only contraceptives and intrauterine devices

REVIEWED RECOMMENDATIONS

ECHO Trial



7,800 women ages 16-35 wanting to prevent pregnancy and willing to be randomized

Randomize
(1:1:1 ratio)

- **DMPA** (2,600 women)
- **LNG implant** (2,600 women)
- **Copper IUD** (2,600 women)

GRADE table for progestogen-only contraceptives

Outcome	Studies	Limitations	Inconsistency	Imprecision	Indirectness	Overall quality	Estimate of effect
DMPA versus non-hormonal contraception							
HIV acquisition	1 randomized trial(3) (7829)^	Few limitations†	No serious inconsistency	No serious imprecision	No indirectness	High	**Adjusted HR 1.04 (0.82-1.33) for DMPA versus Cu-IUD**
Implant versus non-hormonal contraception							
HIV acquisition	1 randomized trial(3) (7829)^	Few limitations†	No serious inconsistency	No serious imprecision	No indirectness	High	**Adjusted HR 1.18 (0.91-1.53) for Cu-IUD versus LNG-implant**
NET-EN versus non-hormonal contraception or no method							
HIV acquisition	6 cohorts studies(5, 33, 35, 36, 38, 39) + 1 individual patient data meta-analysis of 7 studies(40)* (29922)^	Some limitations**	No serious inconsistency	No serious imprecision	No indirectness	Low	Adjusted HR range 0.87 to 1.76, 5 studies increased risk (HR range 1.20 to 1.76), none statistically significant; 2 studies no effect (Adjusted HR range 0.87-1.05). **Pooled adjusted HR 1.14 (0.93-1.39)**.

^Sample size is for the entire study population. † Few limitations note in the trial, but not serious enough to downgrade the level of evidence. While the study was unblinded for participants and health care providers, data was analysed centrally by statisticians who were blinded to the group. *Restricted to studies classified as "informative with but with important limitations".
**Some limitations or imprecision noted across the body of evidence, but not serious enough to downgrade the level of evidence.

GRADE table for Cu-IUD

Outcome	Studies	Limitations	Inconsistency	Imprecision	Indirectness	Overall quality	Estimate of effect
IUD use vs. DMPA							
HIV acquisition	1 randomized trial* (7829) ^	Few limitations†	No serious inconsistency	No serious imprecision	No indirectness	High	**Adjusted HR 1.04 (0.82-1.33) for DMPA-IM versus Cu-IUD**
IUD use vs. Implant							
HIV acquisition	1 randomized trial* (7829) ^	Few limitations†	No serious inconsistency	No serious imprecision	No indirectness	High	**Adjusted HR 1.18 (0.91-1.53) for Cu-IUD versus LNG implant**

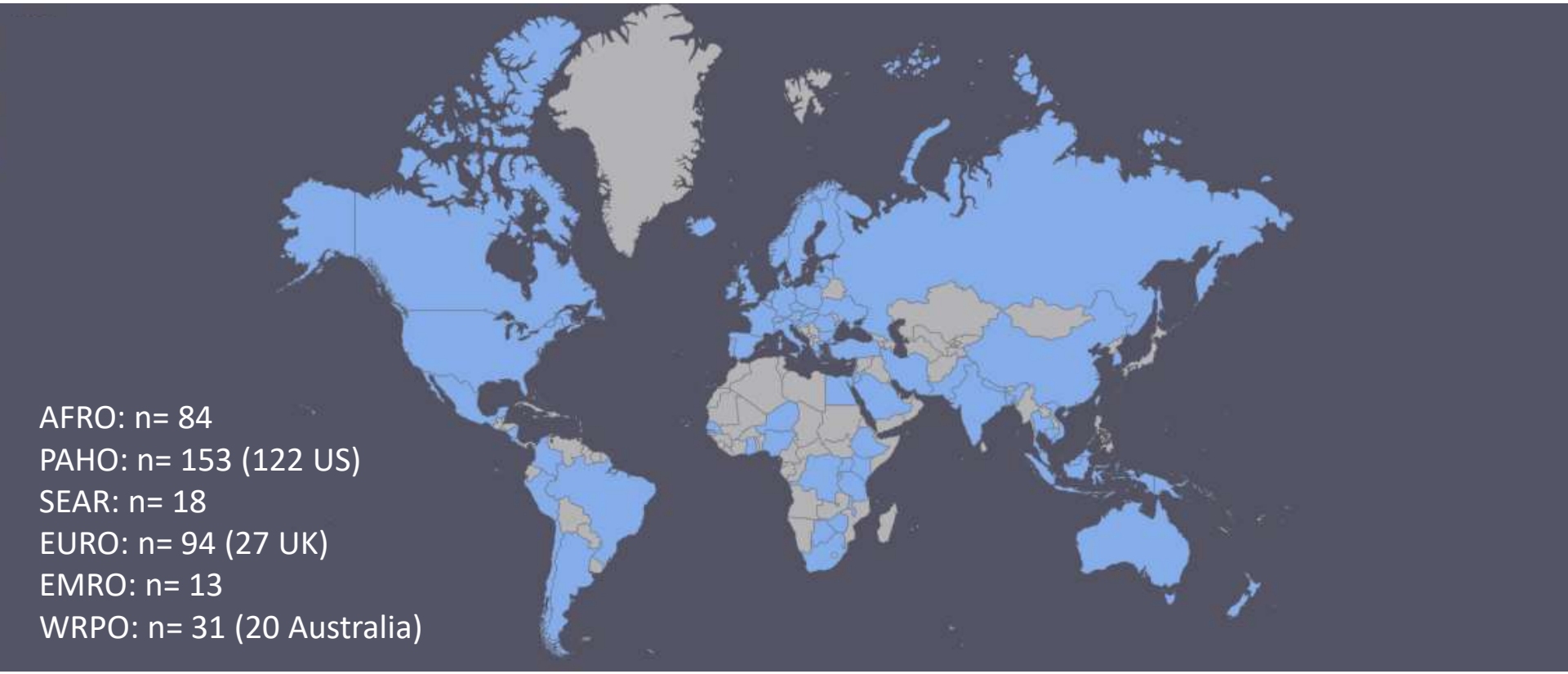
^Sample size is for the entire study population. *Restricted to studies classified as "informative with but with important limitations". † Few limitations noted in the trial, but not serious enough to downgrade the level of evidence

Systematic review, engagement with sex workers, community perspectives

CONTRACEPTIVE VALUES AND PREFERENCES

Systematic Review

- Search results: 375 studies met inclusion criteria

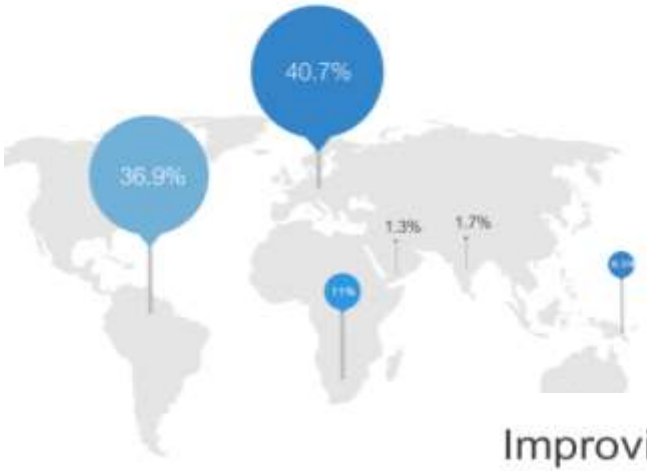


Conclusions

1. Contraceptive users want:
   - A range of contraceptive methods
   - Methods that are efficacious, easy to use, few side effects
   - Control over final method choice, but consultation with providers that emphasizes their values and preferences
   - Comprehensive information about available methods and side effects
2. Wide variability in values and preferences within and across studies
3. Values and preferences shaped by context and available options
   - Counseling can change method choice, but providers may sometimes have incorrect knowledge

Sex worker survey

Regional Distribution of Survey Responses



Most important qualities when choosing a method

Improving contraceptive access: community recommendations

- Address stigma & discrimination in health care settings
- Invest in comprehensive contraceptive education
- Promote community engagement models
- Integrate contraceptive counseling & services
- Prioritize affordability & accessibility
- Acknowledge diversity in gender identity & sexual orientation

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Zimbabwe Qualitative Study

- Participatory focus groups
  - Role play scenarios
- Cost, accessibility, side effects, care at clinics influence use of contraception
- Condom-less sex is common
- Male partners/clients influence contraceptive use

Voices from the HC-HIV advocacy group

- Guidelines work for women when they reflect their concerns – which are diverse and vary.

  "For some women, any level of HIV risk is too much. ECHO does not say that there is 'no risk'."

- Stories from women's lives gathered through extensive community dialogues show that **true contraceptive choice is a myth for many women**

Any changes to the guideline should reflect in clear, straightforward terms, these two critical points.

Biological Data

- Multiple biologic mechanisms could theoretically modify HIV acquisition risk
  - Unclear which are clinically relevant
  - Likely to be multifactorial
- Variable effects by hormone, concentration, mode of administration
- Applicability of data from animal and laboratory studies for clinical outcomes in humans uncertain

EVIDENCE TO DECISION MAKING AND RECOMMENDATIONS

Evidence to decision table: Quality of evidence and benefits vs. harms

Factor	Explanation/evidence		Judgement
Quality of evidence	POCs	High quality for DMPA-IM & LNG implants; low quality for NET-EN; absent for DMPA-SC, LNG IUDs, and ETG implants. NET-EN, DMPA-SC evidence extrapolated from DMPA-IM evidence. LNG implant evidence extrapolated from ETG implants.	High, low or absent depending on method
	IUDs	High quality for Cu-IUD. Evidence absent for LNG-IUDs. For LNG-IUDs, extrapolated from evidence on Cu-IUD and other LNG containing products.	High or absent depending on method
Balance of benefits vs. harms	POCs	Contraception is a life-saving intervention with well-recognized health, social and economic benefits. All POCs and IUDs are highly effective, reversible methods. For DMPA-SC or ETG implants, indirect evidence from DMPA-IM & LNG implants, and no biological or clinical reasons to believe differential HIV risk. For LNG-IUDs, recommendations extrapolated from evidence on Cu-IUDs and other LNG-containing products	Balance is in favor or benefits of POCs
	IUDs		Balance is in favor or benefits of IUDs

Evidence to decision table: Values & preferences, equity & human rights, feasibility

Factor	Judgement
Values & preferences	Support for optimizing informed contraceptive choice and the availability of a wide range of contraceptive options.
Priority of the problem	Effective contraception and HIV prevention are both public health priorities.
Equity & human rights	Recommendations in WHO's human rights guidance are the paramount principles for decision-making on this topic. ➢ Non-discrimination, availability, accessibility, acceptability, quality, informed decision-making, privacy and confidentiality, participation, and accountability.
Feasibility	Clear guidance and a woman-centred approach are essential for successful implementation.

Recommendations for progestogen-only contraceptives

Condition	POP	DMPA/ NET-EN	LNG/ETG	Clarification/evidence
POP = progestogen-only pill LNG/ETG = levonorgestrel and etonogestrel (implants) DMPA = depot medroxyprogesterone acetate (injectable) NET-EN = norethisterone enanthate (injectable)				
High risk of HIV	1	**1**	1	EVIDENCE: High quality evidence from one RCT observed no statistically significant differences in HIV acquisition between: DMPA-IM versus Cu-IUD, DMPA-IM versus LNG implant, and Cu-IUD versus LNG implant (3). Of the low-moderate quality evidence from 14 observational studies, some studies suggested a possible increased risk of HIV with progestogen-only injectable use, which was most likely due to unmeasured confounding (4-6). Low quality evidence from 3 observational studies did not suggest an increased HIV risk for implant users (4-6). No studies of sufficient quality were identified for POPs.

3. Evidence for Contraceptive Options and HIV Outcomes (ECHO) Trial Consortium. HIV incidence among women using intramuscular depot medroxyprogesterone acetate, a copper intrauterine device, or a levonorgestrel implant for contraception: a randomized, multicentre, open-label trial. The Lancet. 2019;394:303-313.

4. Polis CB, Curtis KM, Hannaford PC, Phillips SJ, Chipato T, Kiarie JN, et al. An updated systematic review of epidemiological evidence on hormonal contraceptive methods and HIV acquisition in women. AIDS. 2016;30(17):2665-83.

5. Palanee-Phillips T, Brown ER, Szydlo D, Matovu Kiweewa F, Pather A, Harkoo I, et al. Risk of HIV-1 acquisition among South African women using a variety of contraceptive methods in a prospective study. AIDS. 2019;33(10):1619-22.

6. Sabo MC, Richardson BA, Lavreys L, Martin HL, Jr., Jaoko W, Mandaliya K, et al. Does bacterial vaginosis modify the effect of hormonal contraception on HIV seroconversion. AIDS. 2019;33(7):1225-30.

Recommendations for intrauterine devices

Condition	Cu-IUD	LNG-IUD	Clarifications/evidence
At high risk of HIV	1	1	CLARIFICATION: Many women at high risk of HIV are also at risk of other STIs. For these women, refer to the MEC recommendation on women at increased risk of STIs and the Selected practice recommendations for contraceptive use recommendations on STI screening before IUD insertion (7). EVIDENCE: High quality evidence from one RCT, along with low quality evidence from two observational studies, suggested no increased risk of HIV acquisition with Cu-IUD use (3, 5, 8). No studies were identified for LNG-IUDs.

3. Evidence for Contraceptive Options and HIV Outcomes (ECHO) Trial Consortium. HIV incidence among women using intramuscular depot medroxyprogesterone acetate, a copper intrauterine device, or a levonorgestrel implant for contraception: a randomized, multicentre, open-label trial. The Lancet. 2019;394:303-313.
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7. WHO. Selected Practice Recommendations for Contraceptive Use. Geneva; 2016.
8. Lavreys L, Baeten JM, Martin Jr HL, Overbaugh J, Mandaliya K, Ndinya-Achola J, et al. Hormonal contraception and risk of HIV-1 acquisition: Results of a 10-year prospective study. AIDS. 2004;18(4):695-7.

Implications for policies, programmes and providers

A woman's risk should not restrict her contraceptive choice

Efforts to expand access to contraceptive options must continue

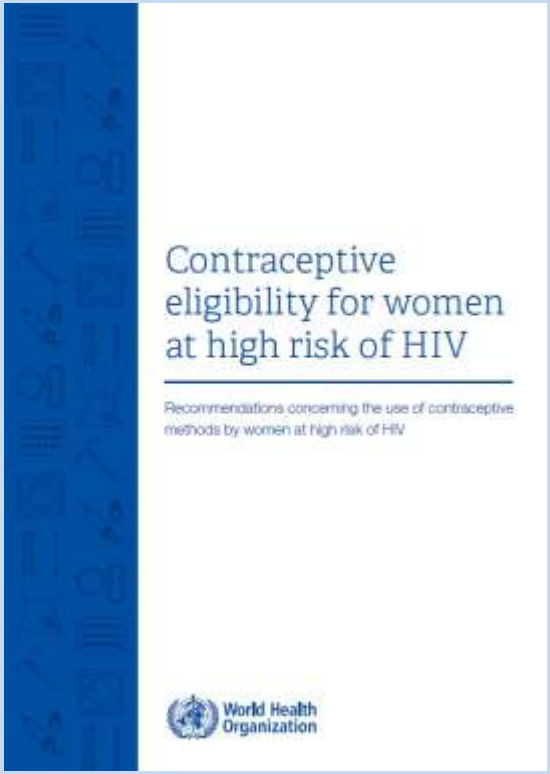
Renewed emphasis on HIV/STI testing services is urgently needed

Integration of family planning and HIV prevention services is essential in high prevalence areas

Low prevalence settings can offer HIV testing and prevention services to women who request them

Conclusions: WHO's updated guidance

For women at high risk of HIV, there are ***no medical restrictions for any contraceptive method***

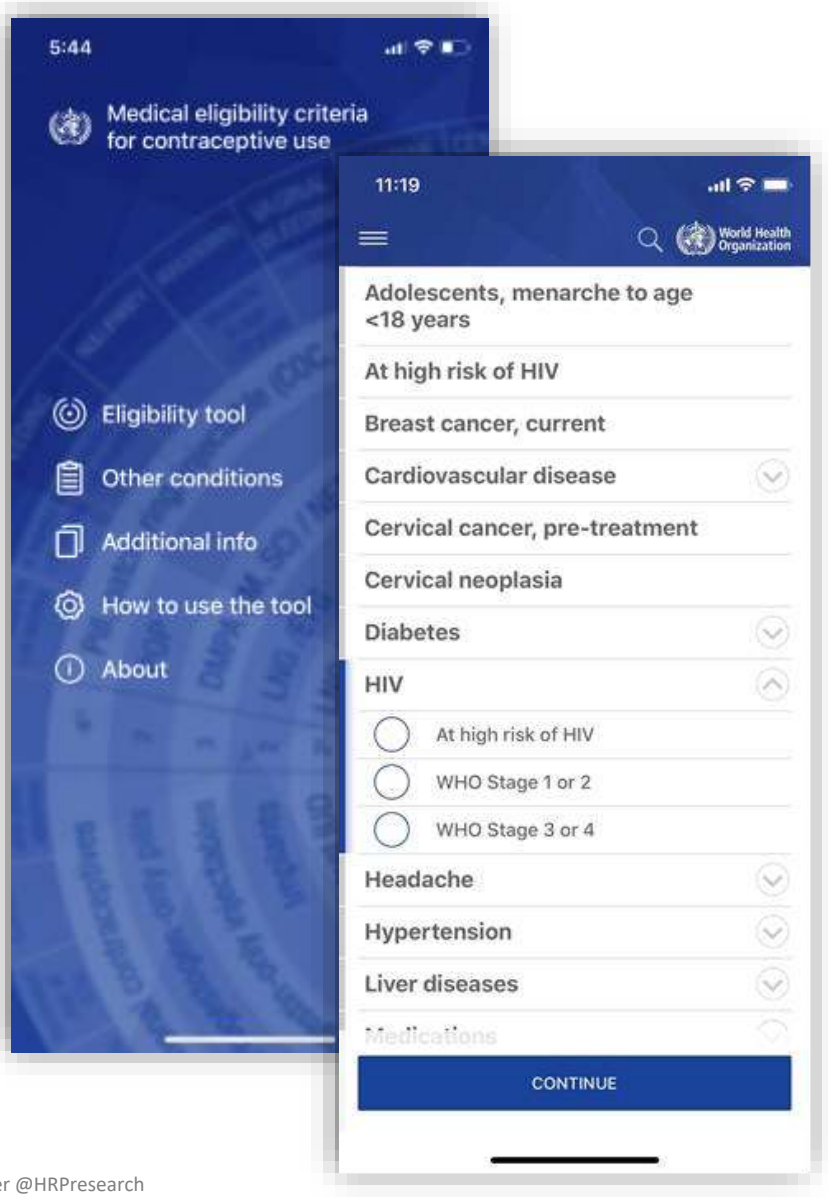


- Progestogen-only contraceptives (pills, injectables, implants)
- IUDs
- Combined hormonal contraceptives (pills, ring, patch, injectable)

https://www.who.int/publications/i/item/9789241550574

https://www.who.int/news/item/29-08-2019-new-app-for-who-s-medical-eligibility-criteria-for-contraceptive-use

MEC app



This update of the Medical eligibility criteria for contraceptive use app provides new recommendations for women who are at high risk of HIV.

Thank You!

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https://www.who.int/teams/sexual-and-reproductive-health-and-research-(srh)